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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/545,772	04/10/2000	Tracy D. Wilkins	420522000100	3347

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EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/545,772	Applicant(s) WILKINS ET AL.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,13-15,19,20,23-26,28-31,33,36-39 and 62-66* is/are pending in the application.

4a) Of the above claim(s) *64-66* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-8,13-15,19,20,23-26,28-31,33,36-39,62 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This Office Action is responsive to Applicant's response filed April 26, 2002. Claims 1-8, 13-15, 19-20, 23-26, 28-31, 33 and 36-39 have been amended. Claims 9-12, 16-18, 21-22, 27, 32, 34-35 and 61 have been cancelled. Claims 62-66 have been added.

2. ***Election/Restriction***

Newly submitted claims 64-66 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Newly submitted claims 64-66, drawn to a method to elicit an immune response in a subject to a pathogenic organism which method comprises administering to a subject in need of such response an effective amount of the immunogenic composition of claims 1, 36 or 37 and are distinct from claims 1-8, 13-15, 19-20, 23-26, 28-31, 33, 36-39 and newly presented claims 62-63, drawn to immunogenic compositions, since the immunogenic composition is a product, where as claims 62-63 are drawn to methods of using that product. In the instant case, the invention of claims 1-8, 13-15, 19-20, 23-26, 28-31, 33, 36-39 and 62-63 and the invention of claims 64-66 are related as product and process of using. For example, the immunogenic composition of claims 1-8, 13-15, 19-20, 23-26, 28-31, 33, 36-39 and 62-63 can be used to produce antibodies. Furthermore, the classification for the immunogenic composition is class 530, subclass 350, while the classification for a method to elicit an immune response,

class 424, subclass 185.1 Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 64-66 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Objections/Rejections Withdrawn

4. In view of Applicant's amendment the following objections and rejections are withdrawn:

a) Objections to the claims are withdrawn, page 2, paragraph 2 of the previous Office action.
b) Rejection of claims 1-19 and 36-39 under 35 U.S.C. 102(b), pages 3-4, paragraph 4 of the previous Office action.
c) Rejection of claims 1-19 and 36-39 under 35 U.S.C. 102(e), pages 6-7, paragraph 6 of the previous Office action.
d) Rejection of claims 20-24 under 35 U.S.C. 103(a), pages 7-8, paragraph 7 of the previous Office action.
e) Rejection of claims 25-26 under 35 U.S.C. 103(a), pages 8-10, paragraph 8 of the previous Office action.
f) Rejection of claims 27-31 under 35 U.S.C. 103(a), pages 10-11, paragraph 9 of the previous Office action.
g) Rejection of claims 31-35 under 35 U.S.C. 103(a), pages 11-12, paragraph 10 of the previous Office action.

Rejection Maintained

5. The rejection under 35 U.S.C. 102(e) is maintained for amended claims 1-8, 13-15, 19-20, 25-26, 28-29, 36-39 and newly presented claims 62-63 as anticipated by Thomas Jr. et al for the reasons set forth pages 4-5, paragraph 5 of the previous Office Action.

The rejection was on the grounds that Thomas, Jr. et al disclose a composition that contains an antigen, a toxin (*Clostridium difficile, C. novyi, C. sordellii, C. perfringens, C. tetani and C. botulinum*) or a fragment or derivative thereof having adjuvant activity in a pharmaceutically acceptable vehicle (i.e. water, a saline solution, phosphate-buffered saline, a bicarbonate solution or a form of a suppository). Thomas, Jr. et al disclose that toxins included in the composition included *C. difficile* toxin A, *C. Difficile* toxin B, both *C. difficile* toxins A and B, or a fragment or derivative thereof. Thomas, Jr. et al disclose that the *C. difficile* toxins contain the repeats which make up the carbohydrate binding domain of toxin A (ARU) or derivatives thereof. Thomas, Jr. et al disclose that the toxins may be recombinant, synthetic or part of a fusion protein which includes a *Helicobactor pylori* urease or polypeptide which facilitates purification of the fusion protein covalently conjugated to an antigen, chemically cross-linked to an antigen or toxoided (i.e. rendered less toxic) (column 3). Thomas, Jr. et al disclose that intranasal administration of antigens give rise to mucosal immune responses in the upper respiratory tract, gastrointestinal and genito-urinary tracts (column 4).

Since the Office does not have the facilities for examining and comparing applicant's immunogenic composition comprising *Clostridium difficile* toxin proteins with the immunogenic composition comprising *Clostridium difficile* toxin proteins of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the immunogenic composition of the prior art does not possess the same material structural and functional characteristics of the claimed immunogenic composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that Thomas Jr. et al disclose *C. difficile* toxins as mucosal adjuvants but does not suggest the use of these adjuvants to elicit responses to polysaccharide antigens. Applicant urges that Thomas Jr. et al describes the antigens

(i.e. the proteins). Applicant further urges that Thomas Jr. et al fails to disclose all of the elements required by the claims.

It is the Examiner's position that there is nothing on the record to show that the prior art does not anticipate the claimed invention. The claims are drawn to an immunogenic composition for eliciting an immune response to a pathogenic organism which composition comprises a recombinant protein and a polysaccharide component, wherein said protein is encoded by a gene from a strain of *Clostridium difficile* and said polysaccharide component is characteristic of pathogenic microorganism, which pathogenic microorganism is other than *C. difficile*. The claims are drawn to a product (i.e. the immunogenic composition). Thomas Jr. et al teach a composition comprising *C. difficile* toxins and antigens. Thomas Jr. et al teach that any antigen which a protective and or therapeutic immune response is desired may be administered with an adjuvant of the invention. Thomas Jr. et al further teach that the antigens include but are not limited to Helicobacters, Campylobacters, *Clostridia*, *Corynebacterium diphtheriae*, *Boredetella pertussis*, influenza viruses, parainfluenza viruses, respiratory syncytial virus, *Borrelia burgdorderi*, Plasmodium, herpes simplex viruses, human immunodeficiency virus, papilloma viruses, *Vibrio cholera*, *Escherichia coli*, measles virus, rubella virus, varicella-zoster virus, mumps, rotavirus, *Shigella* (i.e. polysaccharide component), *Salmonella typhi*, *Neisseria gonorrhoeae* (i.e. polysaccharide component), *Yersina*, *Treponema pallidum*, hepatitis viruses and *Chlamydia* (column 2, lines 57-67 and column 3, lines 1-8). The limitation such as "for eliciting an immune response to a

pathogenic organism" is being viewed as a limitation of intended use. Therefore, the teachings of the prior art anticipates the claimed invention.

NEW GROUNDS OF REJECTIONS NESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the
> subject matter which the applicant regards as his invention.

6. Claim 14 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 14 recite "the said immunogenic composition of claim 1 wherein said immune response comprises an immune response". It is unclear as to what the applicant is referring?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-8, 13-15, 19-20, 23-24, 36-39 and 63 are rejected under 35 U.S.C. 103(a) as unpatentable over Thomas, Jr. et al *(U.S. Patent No. 5,919,463, filed October 16, 1995)* in view of in view of Schneerson et al *(Infection and Immunity, September , 1992, p. 3528-3532).*

Claims 1-8, 13-15, 19-20, 23-24, 36-39 and 63 an immunogenic composition for eliciting an immune response to a pathogenic organism which composition comprises a recombinant protein and a polysaccharide component, wherein said protein is encoded by a gene from a strain of *Clostridium difficile* and said polysaccharide component is characteristic of pathogenic microorganism, which pathogenic microorganism is other than *C. difficile*.

Thomas, Jr. et al disclose a composition that contains an antigen, a toxin (*Clostridum difficile, C. novyi, C. sordellii, C. perfringens, C. tetani and C. botulinum*) or a fragment or derivative thereof having adjuvant activity in a pharmaceutically acceptable vehicle (i.e. water, a saline solution, phosphate-buffered saline, a bicarbonate solution or a form of a suppository). Thomas, Jr. et al disclose that toxins included in the composition included *C. difficile* toxin A, *C. Difficile* toxin B, both *C. difficile* toxins A and B, or a fragment or derivative thereof. Thomas, Jr. et al disclose that the *C. difficile* toxins contain the repeats which make up the carbohydrate binding domain of toxin A (ARU) or derivatives thereof. Thomas, Jr. et al disclose that the toxins may be recombinant, synthetic or part of a fusion protein which includes a *Helicobactor pylori* urease or polypeptide which facilitates purification of the fusion

protein covalently conjugated to an antigen, chemically cross-linked to an antigen or toxoided (i.e. rendered less toxic) (column 3). Thomas, Jr. et al disclose that intranasal administration of antigens give rise to mucosal immune responses in the upper respiratory tract, gastrointestinal and genito-urinary tracts (column 4). Thomas Jr. et al teach that any antigen to which a protective and/or therapeutic immune response is desired may be administered with the adjuvant of the invention (column 2, lines 57-59). Thomas Jr. et al teach the use of C. difficile toxin A and ovalbumin used as a vaccine (column 13, Example V). Thomas Jr. et al teach that the invention may be used to treat patients including but not limited to mammals such as humans, cows, horses, pigs, dogs, cats, sheep and goats (column 3, lines 16-19).

Thomas, Jr. et al do not teach serotype 14 *Streptococcus pneumoniae*.

Schneerson et al teach a conjugate vaccine composed of serotype 14 *Streptococcus pneumoniae* capsular polysaccharide bound to Pertussis Toxin. Schneerson et al teach that serotype 14 *Streptococcus pneumoniae* is one of the common types isolated from patients of all ages with infections caused by *Streptococcus pneumoniae*. Schneerson et al teach that serotype 14 *Streptococcus pneumoniae* capsular polysaccharide does not elicit protective levels of antibodies in infants and children and is a less than optimal immunogen of the 23-valent vaccine for adults. Schneerson et al teach that Pertussis toxin is both a virulence factor and protective antigen of *Bordetella pertussis*. Schneerson et al devised a synthetic scheme to prepare a conjugate of serotype 14 *Streptococcus pneumoniae* and Pertussis toxin.

Schneerson et al further teach that the serotype 14 *Streptococcus pneumoniae*-Pertussis toxin conjugate elicited antibodies in mice to serotype 14 *Streptococcus pneumoniae* at levels estimated to be protective in humans and elicited neutralizing antibodies to Pertussis toxin (see the Abstract).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add the serotype 14 *Streptococcus pneumoniae* capsular polysaccharides of Schneerson et al to the immunogenic composition as taught by Thomas, Jr. et al because Schneerson et al teach that 14 *Streptococcus pneumoniae* capsular polysaccharide is a poor immunogen in humans when administered alone, but conjugating these capsular polysaccharides to proteins enhances their immunogenicity (the entire article). It would be expected barring evidence to the contrary that the addition of serotype 14 *Streptococcus pneumoniae* capsular polysaccharides to *Clostridium* toxin would provide a protective and/or therapeutic response.

8. Claims 1-8, 13-15, 19-20, 25-26, 36-39 and 63 are rejected under 35 U.S.C. 103(a) as unpatentable over Thomas, Jr. et al *(U.S. Patent No. 5,919,463, filed October 16, 1995)* in view of in view of Taylor et al *(Infection and Immunity, September 1993, p. 3678-3687).*

Claims 1-8, 13-15, 19-20, 25-26, 36-39 and 63 an immunogenic composition for eliciting an immune response to a pathogenic organism which composition comprises a recombinant protein and a polysaccharide component, wherein said protein is encoded by a gene from a strain of *Clostridium difficile* and said polysaccharide

component is characteristic of pathogenic microorganism, which pathogenic microorganism is other than *C. difficile*.

Thomas, Jr. et al disclose a composition that contains an antigen, a toxin (*Clostridum difficile, C. novyi, C. sordellii, C. perfringens, C. tetani and C. botulinum*) or a fragment or derivative thereof having adjuvant activity in a pharmaceutically acceptable vehicle (i.e. water, a saline solution, phosphate-buffered saline, a bicarbonate solution or a form of a suppository). Thomas, Jr. et al disclose that toxins included in the composition included *C. difficile* toxin A, *C. Difficile* toxin B, both *C. difficile* toxins A and B, or a fragment or derivative thereof. Thomas, Jr. et al disclose that the *C. difficile* toxins contain the repeats which make up the carbohydrate binding domain of toxin A (ARU) or derivatives thereof. Thomas, Jr. et al disclose that the toxins may be recombinant, synthetic or part of a fusion protein which includes a *Helicobactor pylori* urease or polypeptide which facilitates purification of the fusion protein covalently conjugated to an antigen, chemically cross-linked to an antigen or toxoided (i.e. rendered less toxic) (column 3). Thomas, Jr. et al disclose that intranasal administration of antigens give rise to mucosal immune responses in the upper respiratory tract, gastrointestinal and genito-urinary tracts (column 4). Thomas Jr. et al teach that any antigen to which a protective and/or therapeutic immune response is desired may be administered with the adjuvant of the invention (column 2, lines 57-59). Thomas Jr. et al teach the use of C. difficile toxin A and ovalbumin used as a vaccine (column 13, Example V). Thomas Jr. et al teach that the invention may be used to treat

patients including but not limited to mammals such as humans, cows, horses, pigs, dogs, cats, sheep and goats (column 3, lines 16-19).

Thomas Jr. et al do not teach *Shigella flexneri* Type 2a.

Taylor et al teach a conjugate vaccine comprising *Shigella dysenteria* type 1, *Shigella flexneri* type 2a and *Shigella sonnei* bound to bacterial toxoids (carrier proteins). Taylor et al teach that *Shigella dysenteria* type 1, *Shigella flexneri* type 2a and *Shigella sonnei* administered to mice alone are not immunogenic. Taylor et al further teach that *Shigella dysenteria* type 1, *Shigella flexneri* type 2a and *Shigella sonnei* conjugated to a carrier protein injected into mice subcutaneously in saline solutions elicited serum IgG and IgM antibodies with booster responses. When the *Shigella dysenteria* type 1, *Shigella flexneri* type 2a and *Shigella sonnei* conjugate were adsorbed with alum further enhancement of their immunogenicity was observed (see the Abstract).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add the *Shigella flexneri* 2a capsular polysaccharides of Taylor et al to the immunogenic composition as taught by Thomas Jr. et al because Taylor et al teach that *Shigella flexneri* 2a capsular polysaccharides are poor immunogens when administered alone, but conjugating these capsular polysaccharides to proteins enhances their immunogenicity (the entire article). It would be expected barring evidence to the contrary that the addition of the *Shigella flexneri* 2a capsular polysaccharides to *Clostridium* toxin would provide a protective and/or therapeutic response.

9. Claims 1-8, 13-15, 19-20, 28-29, 36-39 and 62-63 are rejected under 35 U.S.C. 103(a) as unpatentable over Thomas, Jr. et al *(U.S. Patent No. 5,919,463, filed October 16, 1995)* in view of Devi et al *(Proc. National Academy of Science, Volume 88, August 1991, p. 7175-7179).*

Claims 1-8, 13-15, 19-20, 28-29, 36-39 and 62-63 an immunogenic composition for eliciting an immune response to a pathogenic organism which composition comprises a recombinant protein and a polysaccharide component, wherein said protein is encoded by a gene from a strain of *Clostridium difficile* and said polysaccharide component is characteristic of pathogenic microorganism, which pathogenic microorganism is other than *C. difficile.*

Thomas, Jr. et al disclose a composition that contains an antigen, a toxin (*Clostridum difficile, C. novyi, C. sordellii, C. perfringens, C. tetani and C. botulinum*) or a fragment or derivative thereof having adjuvant activity in a pharmaceutically acceptable vehicle (i.e. water, a saline solution, phosphate-buffered saline, a bicarbonate solution or a form of a suppository). Thomas, Jr. et al disclose that toxins included in the composition included *C. difficile* toxin A, *C. Difficile* toxin B, both *C. difficile* toxins A and B, or a fragment or derivative thereof. Thomas, Jr. et al disclose that the *C. difficile* toxins contain the repeats which make up the carbohydrate binding domain of toxin A (ARU) or derivatives thereof. Thomas, Jr. et al disclose that the toxins may be recombinant, synthetic or part of a fusion protein which includes a *Helicobactor pylori* urease or polypeptide which facilitates purification of the fusion

protein covalently conjugated to an antigen, chemically cross-linked to an antigen or toxoided (i.e. rendered less toxic) (column 3). Thomas, Jr. et al disclose that intranasal administration of antigens give rise to mucosal immune responses in the upper respiratory tract, gastrointestinal and genito-urinary tracts (column 4). Thomas Jr. et al teach that any antigen to which a protective and/or therapeutic immune response is desired may be administered with the adjuvant of the invention (column 2, lines 57-59). Thomas Jr. et al teach the use of C. difficile toxin A and ovalbumin used as a vaccine (column 13, Example V). Thomas Jr. et al teach that the invention may be used to treat patients including but not limited to mammals such as humans, cows, horses, pigs, dogs, cats, sheep and goats (column 3, lines 16-19).

Thomas Jr. et al do not teach *Escherichia coli* K1 or *Neisseria meningitides* serogroup B.

Devi et al teach that the capsular polysaccharides of *Escherichia coli* K1 and *Neisseria meningitidis* serogroup B are identical (poly{(2→8)-α-N-acetylneuaminic acid)} or poly(α2-8NeuNAc) and serve as essential virulence factors and protective antigens for both pathogens. Devi et al teach that attempts have been made to induce protective immunity to *Escherichia coli* K1 and *Neisseria meningitidis* serogroup B have been thwarted because poly(α2-8NeuNAc), alone or complexed to outer membrane proteins induced low transient levels of IgM antibodies (page 7175). Devi et al teach that when the capsular polysaccharides of *Escherichia coli* K1 and *Neisseria meningitidis* serogroup B are conjugated to tetanus toxin (a carrier protein) and injected into mice in a saline solution the capsular polysaccharides elicit both poly(α2-8NeuNAc) IgM and

IgG antibodies. Devi et al further teach that re-injection elicited booster responses of both isotypes (T-dependent properties) at dosages applicable for clinical use (page 7178).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add the capsular polysaccharides of *Escherichia coli* K1 and *Neisseria meningitidis* serogroup B as taught by Devi et al to the immunogenic composition as taught by Thomas Jr. et al because Devi et al teach that capsular polysaccharides are poor immunogens when administered alone, but conjugating these capsular polysaccharides to tetanus toxin (carrier proteins) enhances their immunogenicity (the entire article). It would be expected barring evidence to the contrary that the addition of capsular polysaccharides of *Escherichia coli* K1 and *Neisseria meningitidis* serogroup B to the *Clostridium* toxin would provide a protective and/or therapeutic response.

10. Claims 1-8, 13-15, 19, 30-33, 36-39 and 63 are rejected under 35 U.S.C. 103(a) as unpatentable over Thomas, Jr. et al *(U.S. Patent No. 5,919,463, filed October 16, 1995)* in view of Fattom et al *(Infection and Immunity, July 1990, 2367-2374).*

Claims 1-8, 13-15, 19, 30-33, 36-39 and 63 an immunogenic composition for eliciting an immune response to a pathogenic organism which composition comprises a recombinant protein and a polysaccharide component, wherein said protein is encoded by a gene from a strain of *Clostridium difficile* and said polysaccharide

component is characteristic of pathogenic microorganism, which pathogenic microorganism is other than *C. difficile*.

Thomas, Jr. et al disclose a composition that contains an antigen, a toxin (*Clostridum difficile, C. novyi, C. sordellii, C. perfringens, C. tetani and C. botulinum*) or a fragment or derivative thereof having adjuvant activity in a pharmaceutically acceptable vehicle (i.e. water, a saline solution, phosphate-buffered saline, a bicarbonate solution or a form of a suppository). Thomas, Jr. et al disclose that toxins included in the composition included *C. difficile* toxin A, *C. Difficile* toxin B, both *C. difficile* toxins A and B, or a fragment or derivative thereof. Thomas, Jr. et al disclose that the *C. difficile* toxins contain the repeats which make up the carbohydrate binding domain of toxin A (ARU) or derivatives thereof. Thomas, Jr. et al disclose that the toxins may be recombinant, synthetic or part of a fusion protein which includes a *Helicobactor pylori* urease or polypeptide which facilitates purification of the fusion protein covalently conjugated to an antigen, chemically cross-linked to an antigen or toxoided (i.e. rendered less toxic) (column 3). Thomas, Jr. et al disclose that intranasal administration of antigens give rise to mucosal immune responses in the upper respiratory tract, gastrointestinal and genito-urinary tracts (column 4). Thomas Jr. et al teach that any antigen to which a protective and/or therapeutic immune response is desired may be administered with the adjuvant of the invention (column 2, lines 57-59). Thomas Jr. et al teach the use of C. difficile toxin A and ovalbumin used as a vaccine (column 13, Example V). Thomas Jr. et al teach that the invention may be used to treat

patients including but not limited to mammals such as humans, cows, horses, pigs, dogs, cats, sheep and goats (column 3, lines 16-19).

Thomas Jr. et al do not teach *Staphylococcus aureus* type 5 or Type 8 capsular polysaccharides or *Pseudomonas aerginosa*.

Fattom et al teach vaccines composed of *Staphylococcus aureus* type 5 and Type 8 capsular polysaccharides conjugated to *Pseudomonas aerginosa* Exotoxin A. Fattom et al teach that *Staphylococcus aureus* type 5 and type 8 capsular polysaccharides are virulence factors and protective antigens for bacteremia caused by *Staphylococcus aureus*. Fattom et al teach that *Staphylococcus aureus* type 5 and type 8 capsular polysaccharides when injected into mice alone do not elicit a serum antibody response. Fattom et al teach that when *Staphylococcus aureus* type 5 and type 8 capsular polysaccharides are bound to a protein (i.e. *Pseudomonas aerginosa* exotoxin A) to form a conjugate both *Staphylococcus aureus* type 5 and type 8 elicit antibody responses. Fattom et al teach that *Staphylococcus aureus* type 5 and type 8 capsular polysaccharides acquire T-cell dependent properties as shown by their ability to respond to carrier priming and thus stimulate booster responses (see the Abstract).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add the *Staphylococcus aureus* type 5 and type 8 capsular polysaccharides of Fattom et al to the immunogenic composition as taught by Thomas Jr. et al because Fattom et al teach that *Staphylococcus aureus* type 5 and type 8 capsular polysaccharides are poor immunogens in humans when administered alone, but conjugating these capsular polysaccharides to proteins enhances their

immunogenicity both for active immunization and for preparing high-titered antisera in volunteers for passive immunization (page 2368). It would be expected barring evidence to the contrary that the addition of *Staphylococcus aureus* type 5 and type 8 capsular polysaccharides to the *Clostridium* toxin would provide a protective and/or therapeutic response.

Pertinent Prior Art

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Williams (U.S. Patent No. 5,919,665, filed March 16, 1995).*

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
July 10, 2002

MARK NAVARRO
PRIMARY EXAMINER